REMARKS

This Response, filed in reply to the Office Action dated July 27, 2007, is believed to be fully responsive to each point of objection and rejection raised therein. Accordingly, favorable reconsideration on the merits is respectfully requested.

Claims 1-4 and 6-19 are all the claims pending in the application, of which 1-3 and 17-19 are withdrawn from consideration as being directed to non-elected inventions. Claims 4 and 6-16 are rejected. Claims 8, 9, 14 and 15 are canceled. Claims 1, 3, 4, 6, 7 and 17-19 are amended, and support for these amendments can be found throughout the specification, and at least in the working examples provided on pages 20-23 of the originally filed specification. Upon entry of these amendments, Claims 1-4, 6, 7, 10-13 and 16-19 will be all the claims pending in the application. Applicants respectfully request rejoinder of method Claims 17-19 should the generic product claim ultimately be found to be allowable, since these method claims are ultimately dependent from, and thus incorporate all the limitations, of Claim 4.

Claim Objections

On page 2 of the Office Action, Claims 14 and 16 are objected to under 37 CFR § 1.75(c), as allegedly being of improper dependent form for failing to further limit the subject matter of a previous claim.

Solely to advance prosecution, Applicants hereby voluntarily cancel Claim 14, thus rendering moot the objection to Claim 14. Further, Applicants point out that Claim 16 is written in independent form, and thus the objection to Claim 16 is improper.

Accordingly, withdrawal of the objection is respectfully requested.

Claim Rejections - 35 U.S.C. § 112, Second Paragraph

On page 2 of the Office Action, Claim 15 is rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite. The Office Action alleges that recitation of "*Escherichia coli* selection strain is derived from *Escherichia coli* SD840 strain" is interpreted as being a strain that is both strain SD840, and a derivative of SD840.

Applicants respectfully submit that the cancellation of Claim 15 renders the rejection moot.

Withdrawal of the rejection is therefore respectfully requested.

Claim Rejections - 35 U.S.C. § 112, First Paragraph

On page 3 of the Office Action, Claims 4 and 6-13 are rejected under 35 U.S.C. § 112, first paragraph, because the claims allegedly contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The Office Action asserts that the specification discloses a few *E. coli* strains having expression of an exogenous gene encoding a phenylalanine ammonia lyase selected using a stress response index, such as the *E. coli* SD840 strain. However, the Office Action asserts that these strains do not represent all strains recited in the instant claims. Further, the Office Action alleges that the specification neither teaches the structures of all genes nor teaches how all *E. coli* strains will be modified and that the claims as written encompass a large variable genus that Applicants do not disclose how all these strains will be modified to produce the recited function.

To further clarify Applicants' intended invention, Applicants hereby amend Claims 1, 3, 4, 6, 7 and 17-19. Applicants respectfully submit that adequate written description is provided in the originally filed specification for the claims as amended. Specifically, Applicants refer to Example 2 on page 20 of the originally filed specification, which clearly describes the generation of the claimed transformant containing a phenylalanine ammonia lyase gene. Applicants respectfully submit that the amendments to the claims overcome the written description rejection.

Accordingly, withdrawal of this rejection is respectfully requested.

On page 4 of the Office Action, the Office Action rejects Claims 4 and 6-13 under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for *E. coli* strain (SD840), allegedly does not reasonably provide enablement for any *E. coli* strain having expression of any exogenous gene or a genus of *E. coli* strain having expression of phenylalanine ammonia lyase selected using stress response index measured by measuring hydrogen peroxide decomposition.

The Office Action alleges that the specification does not support the broad scope of the claims because the specification does not establish: (A) regions of the DNA structure of a gene which should be modified to control expression and/or to regulate any *E. coli* strain's stress response (B) the general tolerance of *E. coli* stress response and expression in the modification of gene and extent of such tolerance towards the expression of the gene; (C) a rational and predictable scheme for modifying any gene residues with an expectation of obtaining the desired biological function; and / or controlling the gene by any means towards such biological function

(D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. The Office Action concludes that without sufficient guidance, selecting any *E. coli* strain expressed with any exogenous gene is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Initially, to further define Applicants' intended invention, the instant claims have been amended such that recitation of "exogenous gene" has been replaced with "phenylalanine ammonia lyase gene." The test of enablement is whether one reasonably skilled in the art could make or use the invention as claimed from the disclosures in the patent, and the information known in the art, without undue experimentation. Applicants respectfully submit that the claims as amended are clearly enabled, in view of the following remarks.

The strains encompassed by the instant claims are defined by their increased peroxidase-producing phenotype, and as is shown in Examples 4-6 of the originally filed specification, at most only routine experimentation is required to identify *E. coli* strains transformed with a phenylalanine ammonia lyase gene that exhibit increased peroxidase production. Indeed, on page 8 of the Office Action, it is acknowledged that the determination of stress responses by measuring hydrogen peroxide decomposition of known strains is well known to one of ordinary skill in the art.

Further, the finding that each and every novel strain isolated by Applicants (24 strains in total) that exhibit high peroxidase activity also exhibit increased phenylalanine ammonia lyase expression clearly indicates that little or no experimentation is required to identify novel *E. coli*

strains by elevated peroxidase activity that are transformed with a phenylalanine ammonia lyase gene and which exhibit stable and increased expression of phenylalanine ammonia lyase. Thus, from reading the instant specification, one of ordinary skill in the art would understand that strains exhibiting an increased peroxidase activity, as measured by vigorous oxygen production upon addition of hydrogen peroxide, reliably have increased phenylalanine ammonia lyase expression as compared to the parent strain, which does not possess increased peroxidase activity or increased exogenous gene expression. Thus, after taking guidance from the specification, one of ordinary skill in the art would not have to embark on any undue experimentation to make or use the claimed invention. Rather, the only experimentation required is the identification of strains exhibiting high peroxidase activity, which the Office Action admits on page 8, is well known to the skilled artisan.

Applicants respectfully submit that in view of the above remarks, it would not require undue experimentation to generate and identify the claimed *E. coli* strains. Accordingly, Applicants respectfully submit that the specification as filed is fully enabling for the claims as amended.

Withdrawal of the rejection is therefore respectfully requested.

Claim Rejections - 35 U.S.C. 103

On page 10 of the Office Action, Claims 4-15 are rejected under 35 U.S.C. 103(a) as allegedly being obvious over Rowbury *et al.* (*J. appld. Microbiol.*, 2001, 90:677-695) in view of Seaver *et al.* (*J. Bacteriol.* 2001. pp 7182-7189).

The Office Action alleges that Rowbury *et al.* disclose that in cells of microorganisms, such as *E. coli*, "the stress response increases upon expression of exogenous genes (a foreign biological component including antibiotics, bacteriophages etc, page 678 and Table 1)." The Office Action also alleges that Rowbury *et al.* disclose that such stress can be correlated with hydrogen peroxide build-up inside the cell.

Further, the Office Action alleges that Seaver *et al.* disclose the measurement of hydrogen peroxide decomposition activity in growing *E. coli* and that hydrogen peroxide forms in *E. coli* upon stress. In this regard, it is alleged that "it is easier to monitor stress response in *E. coli* by measuring the hydrogen peroxide decomposition."

The Office Action concludes that a person of ordinary skill in the art would be motivated to use the method of Seaver *et al.* to measure hydrogen peroxide decomposition activity to select stressed *E. coli,* wherein an increase in exogenous gene expression is correlated with an increase in the stress response of the *E. coli* as taught by Rowbury *et al.*

Applicants respectfully submit that the claimed invention is not obvious over Seaver *et al.* and Rowbury *et al.* in view of the following remarks.

Specifically, although the Office Action alleges that Rowbury *et al.* disclose that exogenous gene expression results in a stress response, Applicants assert that this result, however, is not actually disclosed, or even suggested by Rowbury *et al.* In this regard, the Office Action refers to Table 1, which discloses three types of biological stresses or agents (antibiotics, bacteriophages and colicins). The only agent in this list that even contains exogenous genes are bacteriophages, however, Rowbury *et al.* do not suggest that stress induced

by bacteriophages is the result of bacteriophage gene expression. Rather, Rowbury *et al.* disclose on page 692 that "phage almost certainly use only extracellular sensors", that is, that the induction of stress caused by bacteriophages occurs whilst the phage is extracellular, and thus before phage entry and gene expression. Accordingly, the only mechanism proposed for stress induction by bacteriophages in Rowbury *et al.* is the activation of an extracellular *E. coli* stress sensor. Therefore, Rowbury *et al.* actually teach away from bacteriophage gene expression inducing stress, by stating that bacteriophages "almost certainly use only extracellular sensors."

As Seaver *et al.* do not disclose that exogenous gene expression in *E. coli* results in a stress response, neither Rowbury *et al.* nor Seaver *et al.*, taken alone or in combination, teach each and every element of the claims, as is required to maintain a rejection under 35 U.S.C. 103(a).

Further, there is no teaching, or even suggestion, within either Rowbury *et al.* or Seaver *et al.* that would lead of one ordinary skill in the art to contemplate that the level of phenylalanine ammonia lyase expression correlates with an increased stress response that can be determined by peroxidase activity of the *E. coli* strain. In view of the above remarks, Applicants respectfully submit that Rowbury *et al.* and Seaver *et al.*, taken alone or in combination, do not render the claimed invention obvious.

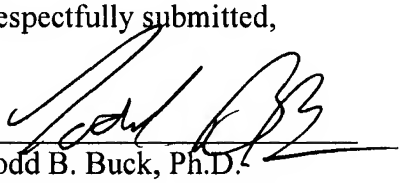
Withdrawal of the rejection is therefore respectfully requested.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the

Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



Todd B. Buck, Ph.D.
Registration No. 48,574

SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860

WASHINGTON OFFICE
23373
CUSTOMER NUMBER

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